

Specification

The amendment filed June 13, 2003 stands objected to under 35 U.S.C. 132 because it allegedly introduces new matter into the disclosure, specifically the alteration of SEQ ID NO: 1. The Examiner states that changes to page 19, lines 2 and line 6 in the Brief Description of the Drawings section describing Figures 1 and 2 are improper.

Although Applicants contend the originally filed Figures 1 and 2 show the first (D) and last (G) amino acid residues of SEQ ID NO:1, which were unintentionally not provided in the Sequence Listing ID dated April 22, 2002, Applicants have now removed the first (D) and last (G) amino acid residues of SEQ ID NO:1 and thus respectfully request that this objection under 35 U.S.C. 132, be withdrawn.

Rejection under 35 USC 112 (second paragraph)

Claims 36-40 stand rejected under 35 USC 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleges that claims 36-40 are vague and indefinite with respect to the recitation in step c. It is allegedly unclear to the Examiner what criteria are used in comparing the mass spectrum profile of peptides isolated from the sample to the mass spectrum profile of a peptide having SEQ ID NO: 1. The Examiner questions does this mean 100% match? Is it the same to say that detection of SEQ ID NO:

1 in the patient sample is diagnostic for myocardial infarction? Additionally, the Examiner contends that the claims are confusing because it is unclear what "characteristics" are used as the basis of comparison. These characteristics are purportedly not clearly defined.

Claim 36 has been amended to remove the phrases "characteristic" and "diagnostic" and these limitations are not recited in any of the remaining pending claims.

Additionally, Applicants have amended the claims to clearly and concisely claim the presence of said isolated biopolymer marker having SEQ ID NO: 1 in the sample displaying a peak profile at about 1350 Da in the mass spectrum being indicative of a link to renal failure or myocardial infarction. This does not require 100% match or other characteristics for a basis of comparison, it simply requires a peak be present at about 1350 DA, which evidences a link to renal failure or myocardial infarction. The instant specification fully supports the disease specific marker identified by the SEQ ID NO: 1, characterized as Alpha Fibrinogen, having a molecular weight of about 1350 daltons as set forth in Figure 2 being indicative of an individual suffering from renal failure or myocardial infarction, see page 27, lines 17 to page 28 to line 2.

The Examiner next asserts that claims 36-40 are vague and indefinite because it is unclear how one may "positively identify" a patient as suffering from either renal failure or myocardial infarction or both, by the identification of a mass spectrum

profile of peptides in a sample that displays the characteristic profile of the mass spectrum profile of SEQ ID NO: 1.

Applicants point Examiner's attention to the instant specification on page 16, line 19 to page 17, line 6 that states subsequent to the isolation of particular disease state marker sequences as taught by the instant invention, the promulgation of various forms of risk-assessment tests are contemplated which will allow physicians to identify asymptomatic patients before they suffer an irreversible event such as diabetes, kidney failure, and heart failure, and enable effective disease management and preventative medicine. In other words, after identifying the mass spectrum peak profile of SEQ ID NO: 1 in a patient sample by the present method, the patient's disease is positively identified through other various risk-assessment tests.

Routine risk-assessment tests generally include blood and urine analysis, x-rays, electrocardiogram (EKG), cardiac stress tests, computer assisted tomography (CAT) scans, magnetic resonance imagery (MRI), echocardiographic studies, Doppler analysis, angiograms, electromyograph (EMG), electroencephalograph (EEG) and the like, and are well known in the diagnostic art to assist physicians in forming a definitive diagnosis, see paragraph bridging page 1 and 2 in Applicant's co-pending application no. 09/846,330, now Pub. No. U.S. 2002/0160420, both applications were filed on April 30, 2001.

Additionally, in response to the Examiner's assertions during

the interview of October 21, 2004, Applicants herein provide a Declaration under 37 CFR 1.132 with attached Appendix A. Appendix A was originally filed in Applicant's application no. 09/846,330. Appendix A illustrates data obtained from a study of over 500 patients suffering from a variety of disease states. The specification of 09/846,330 literally states at page 32, lines 9 to 15;

Appendix A clearly illustrates patient specific samples obtained and the data used to formulate a library of proteomic materials having characteristics identifiable with both normal and abnormal physiological conditions or predictive hallmarks thereof. Data which is exemplary of the information retrieved via the novel proteomic investigative techniques of the instant invention are set forth in Appendix A.

During the interview the Examiner questioned whether the number of patients e.g. 16 patients in FIGURE 1, some of which were tested more than once, is adequate to conclude myocardial infarction or renal failure. Appendix A clearly illustrates a patient history, disease and protein name, molecular weight and the identified peptide sequence associated with the disease. The data set illustrated in FIGURE 1 of the instant application can be found on pages A3 to A4 of Appendix A at MW 1350.

Accordingly, Applicants have now clarified the metes and bounds of the claims and respectfully request that the above-

discussed rejections under 35 USC 112 (second paragraph) be withdrawn.

Rejection under 35 USC 112 (first paragraph)

Claims 36-43 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The claims allegedly contain subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time of the application, had possession of the claimed invention. The Examiner states the invention as currently amended is different from what is defined in the claim(s) and original specification because nothing in the specification leads one to predict that the peptide of SEQ ID NO: 1 comprises 15 amino acids with the first and last being Asp (D) and Gly (G), respectively.

As discussed above with respect to the objection to the specification, Applicants maintain that originally filed Figures 1 and 2 clearly disclose the first and last amino acid residues of SEQ ID NO: 1 as listed in Sequence Listing filed June 13, 2003, and thus, not new matter. However, Applicants have now removed the first (D) and last (G) amino acid residues of SEQ ID NO:1 and thus respectfully request that this rejection be withdrawn.

With respect to previously added claims 41-43, which recite a test kit comprising an antibody that binds to a peptide consisting of amino acid residues 2-14 of SEQ ID NO. 1 in the sample of a patient and a biopolymer marker peptide consisting of amino acid

residues 2-14 of SEQ ID NO. 1, the Examiner alleges that such a test kit is not supported by the specification. Although Applicant maintain that such test kits are fully supported by the specification as originally filed, claims 41-43 drawn to a test kit have been herein cancelled rendering this rejection moot.

Previously added claims 36-40 stand rejected as containing subject matter which was allegedly not described in such way as to reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention. Specifically, claims 36-40 recite a method for diagnosing myocardial infraction or renal failures by detecting a biopolymer marker from a patient sample and comparing the detected marker to the biopolymer marker having SEQ ID NO: 1. The Examiner alleges that while the specification does disclose how a biopolymer marker of identified as SEQ ID NO: 1 was identified from patient serum samples at pages 26 to 31, nowhere in the specification is there a teaching of detecting any other biopolymer marker and comparing the detected marker to SEQ ID NO. 1 and determining a disease state from the detected marker.

Moreover, the Examiner indicates there is no nexus between the procedure for screening samples from patients having a variety of different diseases and determining that SEQ ID NO: 1 is diagnostic for myocardial infarction (MI) or renal failure.

The Examiner indicates there is no clear teaching in the specification, that after having detected SEQ ID NO. 1 in a sample,

one may then definitively diagnose a patient as either suffering from MI or renal failure or both. The Examiner alleges that there is no disclosure in the specification regarding further testing of patients suspected of having MI or renal failure or both, in which the claimed peptide is present, followed up by a diagnosis of MI or renal failure by the use of other diagnostic methods.

Applicants respectfully disagree with the Examiner's above mentioned arguments since the specification does state on page 16, line 19 to page 17, line 6 that subsequent to the isolation of particular disease state marker sequences, as taught by the instant invention, the promulgation of various forms of risk-assessment tests are contemplated which will allow physicians to identify asymptomatic patients before they suffer an irreversible event such as diabetes, kidney failure, and heart failure, and enable effective disease management and preventative medicine. Routine risk-assessment tests generally include blood and urine analysis, x-rays, electrocardiogram (EKG), cardiac stress tests, computer assisted tomography (CAT) scans, magnetic resonance imagery (MRI), echocardiographic studies, Doppler analysis, angiograms, electromyograph (EMG), electroencephalograph (EEG) and the like, and are well known in the diagnostic art to assist physicians in forming a definitive diagnosis, see related application serial number 09/846,330, paragraph bridging page 1 and 2.

Thus, Applicants respectfully submit that the specification does in fact teach that patients suspected of having MI or renal

failure or both in which the claimed peptide was found to be present was followed up, or confirmed, by a diagnosis of MI or renal failure utilizing other routine diagnostic tests. However, the intended purpose of the invention is to provide improved, alternative means for diagnosis of MI or renal failure which can easily be performed by an untrained individual without the need for additional testing. If "follow up" diagnostic methods are also required, then the diagnostic process is lengthened and the invention fails to fulfill its intended purpose. Therefore, Applicants respectfully submit that this rejection be withdrawn.

Further, Applicants direct Examiner's attention to attached Appendix A which illustrates data obtained from screening samples from over 500 patients having a variety of different diseases, e.g. stroke, CHF, insulin resistance, etc. For example, in patient (# SJ CON 07) a fragment (DFLAEGGGVR) of SEQ ID NO: 1 (SESDFLAEGGGVR) was positively identified through the instant method, see row 1 from top on page A1. In this same patient (# SJ CON 07) the biopolymer marker having SEQ ID NO: 1 was also positively identified, see page A3 columns 11 and 12 from bottom, thereby indicating a link between the presence of biopolymer having SEQ ID NO: 1 and/or a fragment thereof with a diagnoses of MI and/or renal failure.

Claims 36-40 also stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art

to which it pertains, or with which is most nearly connected, to make and/or use the invention.

Claims 36-40 recite a method for diagnosing myocardial infraction or renal failures by detecting a biopolymer marker from a patient sample and comparing the detected marker to the biopolymer marker having SEQ ID NO: 1, the Examiner alleges such a method is not enabled by the specification as originally filed.

The guidelines for a "test of enablement" indicate that if a statement of utility in the specification contains within it a connotation of how to use, 35 USC 112 is satisfied. Furthermore, it has been established that the mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it. The instant application discloses a peptide (SEQ ID NO:1) which is related to MI and/or renal failure, such a peptide has not previously been shown to be related to MI and/or renal failure. When a peptide is discovered to be associated with a disease state it carries with it a connotation of potential diagnostics and/or therapeutics. Thus, based upon the statements made in the instant paragraph, the test for enablement is not sufficient to support an enablement rejection.

Although Applicants believe that the instant specification fully supports the claim that an isolated peptide consisting of SEQ ID NO:1 is diagnostic for MI and/or renal failure, in the interest of efficient prosecution Applicants have amended the claim(s) to

recite that the isolated peptide is linked to MI and/or renal failure.

According to dictionary.com the term "linked" refers to the condition of being associated with or connected to (see attached). The instant specification fully supports a connection and/or an association of the claimed peptide with MI or renal failure. The instant specification states on page 17, lines 11 to 14 as an objective of the instant invention the evaluation of samples containing a plurality of biopolymers for the presence of disease specific marker sequences which evidence a link to at least one specific disease state. The data presented in the figures further supports the association of the claimed peptide with MI or renal failure.

The Examiner asserts there is nothing specific in the procedure which would enable one to chose SEQ ID NO: 1 as a notable sequence among all the possible protein or peptides in the sample, and determine that SEQ ID NO:1 is diagnostic for MI or renal failure.

The Examiner states that a number of characteristics need to be considered in the development of any suitable diagnostic assay. These characteristics, upon which the Examiner appears to rely, are found in Strongin (1993, "Sensitivity, Specificity, and Predictive Value of Diagnostic Tests: Definitions and Clinical Applications", in Laboratory Diagnosis of Vial Infections, Lennette, e., ed. Marcel Dekker, Inc. New York, pp. 211-219), which is allegedly relevant to

the instant invention. The Strongin reference describes a set of statistical characteristics that a clinician can apply to confirm or exclude the diagnosis of disease. Each of the diagnostic procedures possesses a set of characteristics that determine how close the procedure in question compares to an "ideal" test, that is, one with 100% specificity and sensitivity, which as the text states is extremely uncommon.

The Examiner appears to believe that since the specification allegedly lacks any teaching of how the diagnostic test were preformed, or any information regarding the patients from which the samples were taken, and whether any considerations were given to any of the statistical characteristics stated in the reference, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

Applicants respectfully disagree with the Examiner's assertions. The skill in the art is high and it is obvious that no undue experimentation would be required for a skilled artisan to follow any of the protocols presented in the instant specification, since these protocol are well known in the art.

What is conventional or well known to one of ordinary skill in the art not be disclosed in detail. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94. A patent need not teach, and preferably omits, what is well known in the art (see MPEP 2164.01). If a skilled artisan would have understood the inventor to be in possession of the claimed

invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, the adequate description requirement is met. See, e.g., *Vas-Cath* 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d at 746, 751, 172 USPQ 391, 395 (CPA 1972) (stating "the description need not be in *ipsis verbis* to be sufficient"). See MPEP 2163 (3).

Assuming *arguendo* that specific protocols were not included within the disclosure, Applicants do not agree that all diagnostic tests must specifically disclose the maximum sensitivity desired, specificity desired and efficiency desired, and other statistical analysis, as set forth in the Strongin reference, in order to meet the enablement requirement. The data in Figure 1 and herein attached Appendix A do in fact disclose information regarding the patients from which the samples were taken, i.e. gender, age, disease. Furthermore, the specification does disclose how the diagnostic tests were performed in the Background of the Invention section. This section discusses various prior art mass spectrometer formats for use in analyzing the translation products of the present invention, see page 2, line 13- page 4, line 4. The specification discloses that the mass of the target polypeptide determined by mass spectrometry is then compared to the mass of a reference polypeptide of known identity.

The Examiner asserts that the data presented in Figure 1 is not convincing, nor does it clearly demonstrate that SEQ ID NO:1 is indicative of myocardial infarction (MI) or renal failure.

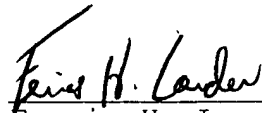
In response to the Examiner's assertion, Applicants previously submitted a Declaration (and Figure) under 37 CFR 1.132, filed October 03, 2003. The figure attached to the declaration provides side-by-side profiles (obtained using techniques of mass spectrometry) of normal human sera versus sera from patients having a history of myocardial infarction. This profile comparison clearly evidences the absence of the 1350 Dalton marker (SEQ ID NO: 1) in normal human sera and thus establishes the specificity of the 1350 Dalton peptide as a biopolymer marker which when present in the sera is diagnostic for myocardial infarction or renal failure.

In conclusion, Applicants claim that the presence of SEQ ID NO:1 is a positive indicator of myocardial infarction and/or renal failure; a statement which is enabled by the data presented in figure 1 and Appendix A. Applicants assert that one of ordinary skill in the art when reviewing the instant specification and declaration filed herewith would recognize how to use the claimed peptide as a marker for myocardial infarction. Thus, Applicants respectfully request that this rejection under 35 U.S.C. 112, first paragraph now be withdrawn.

CONCLUSION

In light of the foregoing remarks, amendments to the specification and amendments to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



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